

**Model-based diagnosis of acute pulmonary embolism and septic shock in porcine trials.**

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Acute pulmonary embolism (APE) and septic shock (SS) are prevalent dysfunctions in the intensive care unit (ICU) and are associated with high rates of mortality. The aim of this research is to test the ability of a model-based technique to diagnose and track disease-dependent hemodynamic changes resulting from these forms of shock.

In two porcine studies, APE (N=5) and SS (N=4) were induced using autologous blood clot injections and endotoxin infusions, respectively. In both studies hemodynamic measurements were recorded every 30 minutes. Subject-specific cardiovascular system (CVS) models were fitted to each pig from a minimal set of typically available ICU measurements. Identified parameters and outputs were compared to experimentally derived indices, measurements not used in the identification, and trends from the literature to validate the subject-specific models.

The models accurately predicted the maximum ventricular pressures and end diastolic ventricular volumes to mean absolute errors of less than 7.1% and 6.7%, in both studies. Modelled pulmonary vascular resistance (PVR) compared well ( $R=0.68$  for APE and  $R=0.73$  for SS) to the experimentally derived values. Importantly, in the APE study a large rise in PVR, a major hemodynamic consequence of APE, was identified in all five pigs as expected. In response to endotoxin infusion a drop in systemic vascular resistance of 26% (on average) was identified by the model, in contrast to an increase seen in the APE pigs. In addition, hyperdynamic states were observed in two of the pigs, consistent with known trends for septic shock.

These results indicate that subject-specific CVS models can be used to diagnose APE and SS. Furthermore, the identified models can accurately monitor acute hemodynamic changes resulting from these two common forms of shock, indicating the potential for the model to be used as assistive tool for therapy decisions.